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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PRIEBE, SCOTT DAVID	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 10/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/506,327	HIRAMATSU ET AL.	
	Examiner	Art Unit	
	Scott D. Priebe, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *1-20,40 and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-28* is/are rejected.

7)☒ Claim(s) *29-39* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20040902,20050831,20051021*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II, claims 21-39 in the reply filed on 9/11/06 is acknowledged. The traversal is on the ground(s) that since claim 40 depends from claim 21, it is improper to restrict between groups II and III. This is not found persuasive because under PCT Rule 13.3, lack of unity of inventions does not depend on the manner in which the inventions are claimed, i.e. restriction may be made within and between claims where unity of invention is lacking. The restriction requirement of 8/16/06 provides reasons why groups II and III do not share a special technical feature. As indicated in the restriction requirement of 8/16/06, the product of claim 40 reads on products described in the prior art. Applicant also suggests that if the inventions lack unity of invention, Applicant should be afforded the opportunity to revise the claims prior to restriction. Applicant provides no basis for this assertion. Applications when filed should be limited to a single invention, and ready for examination on the merits. There is no provision in under either PCT rules or 37 C.F.R. for what Applicant suggests. Furthermore, Applicant did have the opportunity to amend the claims in response to the restriction requirement, but failed to take that opportunity.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-20, 40, and 41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9/11/06.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. However, it is noted that Applicant cannot rely upon the foreign priority papers to overcome any rejection made under 35 USC 102 or 103 because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Information Disclosure Statement

Documents BA and BB of the IDS filed 8/31/05 and document BA of the IDS filed 10/21/05 were considered to the extent of the information present their English abstracts, the remainder of the documents being in a language other than English. Document CB of the IDS filed 9/2/04 could be considered only to the extent that it was identified on the search report as a Y reference with respect to claims 1-41, since only the bibliography of the document was in English. The respective search reports provide no information as to how these documents are relevant to the claimed subject matter or why they were cited or what second document(s) they would be combined with to show lack of an inventive step.

Documents CA-CD of the IDS filed 8/31/06 and document CB of the IDS filed 9/2/04 have been considered. However, the PTO-1449 fails to comply with 37 CFR 1.98(b)(5), which requires that each non-patent publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, date, and place of publication (e.g. journal title). The citations for documents indicated above are incomplete since

the titles of articles CA-CD of the IDS filed 8/31/06 and the publication date of document CB of the IDS filed 9/2/04 are not provided on the PTO-1449 forms. Consequently they have been crossed off of the PTO-1449 forms as being unsuitable for printing on the face of the patent. Should Applicant wish these documents to be printed on the face of a patent, under 37 CFR 1.97(f) Applicant should provide a supplemental PTO-1449 listing documents indicated above including complete citations as required under 37 CFR 1.98(b)(5) in the response to this Office action.

It is suggested that the supplemental PTO-1449 list only the documents indicated above. If any new documents other than those listed in the PTO-1449 of 9/2/04 or 8/31/05 are included on the supplemental PTO-1449 or the supplemental PTO-1449 is not provided in response to this Office action, then the requirements of 37 CFR 1.97(c) or (d), as applicable, must be met.

Claim Objections

Claims 29-39 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may not depend from another multiple dependent claims, and also must depend from multiple claims in the alternative only. Each of claims 29-39 is or depends from a multiple dependent claim that depends from a multiple dependent claims, and claim 39 also depends from multiple claims in other than the alternative. See MPEP § 608.01(n). Accordingly, the claims 29-39 not been further treated on the merits.

Claims 21-26 are objected to because of the following informalities: Claim 21, line 4; claim 22, lines 4 and 11; claim 23, lines 4 and 7; claim 24, line 4; claim 25, line 4; and claim 26,

line 3, each recite "of fibroin H chain gene". This phrase is grammatically improper as "fibroin ... gene" lacks an article, e.g. --a-- or --the--. Also, in claim 23, line 7, "fibrin" is misspelled; it should be --fibroin--. Finally, "SEQ. ID No." recited in claims 26 and 28 should be --SEQ ID NO:--. Appropriate correction is required.

Applicant is advised that should claim 24 be found allowable, claim 25 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 25 simply recites a limitation that is inherent to the fibroin H chain gene region recited in claim 24, that the fusion of the first and second exons occurs in the secretion signal region. Consequently, it is of the same scope as claim 24.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 21-28 are directed to a gene cassette that comprises the 5' terminal portion and/or 3' terminal portion "of fibroin H chain gene" and a promoter active in silk glands. As recited in the claims, the "fibroin H chain gene" is generic with respect to the source organism for the required fibroin H chain gene sequences, i.e. the gene might be isolated from any lepidopteran. However, the specification provides only sequences from the fibroin H chain gene of *Bombyx mori*. The genomic sequence of the fibroin H chain structural gene from strain p50 of *Bombyx mori* and about 60 kb of sequence upstream of it was known in the prior art (e.g. see GenBank Acc. No. AF226688). However, there is no evidence of record that these regions of fibroin H-chain genes from any other organism had been cloned or sequenced. Consequently, there is no evidence of record that Applicant was in possession of a genus of expression cassettes comprising the 5' terminal portion and/or the 3' terminal portion of a generic fibroin H chain gene, as claimed, one of skill in this art would not accept that Applicant had adequately described or been in possession of the claimed genus.

Similarly, the promoter as recited may be active in any silk glands from any organism, not only active in *B. mori*, but also in various other moth and butterfly larvae or in spiders or other arthropods that produce silk. In contrast, the specification describes only promoters active in *B. mori* silk glands, and it is unclear whether promoters active in silk glands in other arthropods were even known.

This rejection would be overcome by limiting the fibroin H chain gene(s) to those of *Bombyx mori* and the promoter to one active in *B. mori* silk glands.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 22 as written, it is unclear whether the second recited "gene cassette" (line 6) is an alternative to the "gene cassette" recited in line 1, or an alternative to the "gene" recited in line 3. As a result, the metes and bounds of claim 22 and its dependent claims is unclear. If the former was intended, then 1) a colon should be inserted after "comprising" (line 2) and ", or a gene cassette ... comprising" (lines 6-7) should be replaced with --; or--. Applicant should also reformat the claim using indents to further emphasize the two alternative gene cassettes.

In claim 23, it is unclear if "the 5' terminal portion of fibroin H chain gene" (*sic*) and "the 3' terminal portion of fibrin H chain gene"(*sic*) are from the same "fibroin H chain gene" or may be from different fibroin H chain genes due to the improper grammar indicated above under Objections. This grounds of rejections also applies to claims dependent on claim 23.

Claims 26 and 28 are indefinite for recitation of "the promoter ... and the 5' terminal portion ... are the DNA" (claim 26) and "the 3' terminal portion ... is the DNA" (claim 28). Claims 21-23, from which claims 26 and 28 depend, recite that the "cassette" comprises the promoter, 5' terminal portion, and/or 3' terminal portion. The juxtaposition of open language, i.e. "comprising" in the base claims and the closed language, "are" or "is" in claims 26 and 28 renders the scope of claims 26 and 28 ambiguous. It is unclear whether the claim excludes

additional sequences from the promoter plus 5' terminal portion or from the 3' terminal portion not found in the recited SEQ ID NOs. For example, it is unclear whether a cassette comprising SEQ ID NO: 22, 23, or 24 and additional sequences adjacent to SEQ ID NOs: 22, 23, or 24 in the *B. mori* fibroin H-chain gene is embraced by claims 26 or 28 or not.

Claim 26 recites that the "promoter" and the "5' terminal portion" "are the DNA shown in SEQ. ID No. 22 and SEQ. ID No. 23". As written, these combinations of limitations do not make sense. The last 1396 nucleotides of SEQ ID NO: 23 is SEQ ID NO: 22, which contains the promoter (or at least a functional part of it), exon 1, intron 1, and the first 63 nucleotides of exon 2 of the *Bombyx mori* (strain p50) fibroin heavy chain gene (see Zhou et al., Nucleic Acids Res. 28(12): 2413-2419, at page 2413, col. 2, and page 2415, col. 1, in conjunction with GenBank Acc. No. AF226688, cited therein.). Since both SEQ ID NO: 22 and 23 contain both a promoter active in silk glands and the same 5' terminal portion of the fibroin H-chain transcription unit, it is unclear whether only one of these or both SEQ ID NOs: 22 and 23 are supposed to be the "promoter" and the "5' terminal portion". If both, it is unclear which of SEQ ID NO is supposed to be the "promoter" and which is supposed to be the "5' terminal portion". If Applicant's intention was that either SEQ ID NO: 22 or SEQ ID NO: 23 is both the promoter and 5' terminal portion, then it is suggested that "wherein ... SEQ. ID No. 23" be replaced with:

-- wherein the promoter and the 5' terminal portion together comprise the DNA shown as SEQ ID NO: 22 or SEQ ID NO: 23 --

Claim 26, as it depends from claim 23, is even more unclear since claim 23 may recite two different promoters and 5' terminal portions (see above) and it is unclear as to which of

these the SEQ ID NOs recited in claim 26 refer, i.e. there is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21-25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhao et al. (Acta Biochimica et Biophysica Sinica 33(1): 112-116, Jan. 2001) as evidenced by Zhang et al. (Acta Biochimica et Biophysica Sinica 31(2): 119-123, 1999) and GenBank Acc. No. AF226688. A English translation of Zhao has been attached to the original document, and the discussion of Zhao below refers to the pages of the translation.

Zhao discloses a transgenic silkworm with a genome comprising a "gene cassette" embraced by the instant claims, which do not exclude a gene cassette as present in a transgenic organism, for example. The gene cassette comprises, in order, the 5' end of the endogenous fibroin H-chain gene, including the promoter, exon 1, intron I, and the 5' end of exon II terminated by a PstI site, fused in-frame to a GFP coding sequence, fused in frame to coding sequence for a synthetic fibroin like sequence, fused in frame to a 3' terminal portion of the endogenous fibroin H-chain gene, comprising the three Cys residues, and the endogenous genomic sequence flanking the 3' end of the Fib-H coding sequence. The GFP and fibroin-like coding sequences were inserted into the endogenous gene by gene targeting using the pUC53

vector of Zhang, such that the coding sequence for the repetitive regions of the Fib-H protein were replaced by the exogenous protein structural genes. See entire document, especially Section 2.2 and Fig. 1 (page 5), Fig. 2, and Fig. 5.

Zhang describes pUC53, and indicates that the 5' Fib-H targeting arm (5' flanking sequence) is the XhoI-PstI fragment that begins within intron I and extends into exon II (these sites correspond to the XhoI site at position 62922, and the PstI site at position 63854 of AF226688). The 3' end of instant SEQ ID NO: 22 and 23 corresponds to position 63153 of AF226688. The identity of the 3' targeting arm is less clear. However, Section 1.2.1 shows primers used to detect this sequence. The first primer (downstream of the MluI site, which is not present in the fib-H gene) is identical to the 17 nucleotide sequence beginning at position 78895 of AF226688, while the complement of the second primer is identical to the 17 nucleotides of AF226688 beginning at position 79141, which is the beginning of an EcoRI site. Section 2.2 and Fig. 2 indicate that this EcoRI site is over half-way downstream in the 3' targeting arm, which is 350 nucleotides in length, i.e. the 3' targeting arm extends over 175 nucleotides upstream of the EcoRI site. The MluI site in the first primer appears to correspond to the MluI site inserted into pUC19 in the construction of pUC53. Consequently, it appears that the 3' targeting arm begins at position 78895 of AF226688 and extends about 350 nucleotides downstream to about position 79245. Instant SEQ ID NO: 24 corresponds to positions 79099-79197, and so would correspond to the central region of the 3' targeting arm of pUC53.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 26 and 28 are rejected under 35 U.S.C. 102(b) as anticipated by, as applied to claims 21-25 and 28 above; or, in the alternative, under 35 U.S.C. 103(a) as obvious over Zhao et al. (Acta Biochimica et Biophysica Sinica 33(1): 112-116, Jan. 2001) as evidenced by Zhang et al. (Acta Biochimica et Biophysica Sinica 31(2): 119-123, 1999) and GenBank Acc. No. AF226688, as applied to claims 21-25 and 28 above, and further in view of Zhou et al., Nucleic Acids Res. 28(12): 2413-2419, which cites and is cumulative over GenBank Acc. No. AF226688. This rejection is necessitated by the ambiguity of claims 26 and 28 (see rejection under 35 USC 112, second para. above), which can be interpreted as reading on a gene cassette wherein the promoter plus 5' terminal portion comprises SEQ ID NO: 22 or 23 or the 3' terminal

portion comprises SEQ ID NO: 24, and may comprise additional sequences that flank these in the genome of *B. mori.*

Zhao et al. (Acta Biochimica et Biophysica Sinica 33(1): 112-116, Jan. 2001) as evidenced by Zhang et al. (Acta Biochimica et Biophysica Sinica 31(2): 119-123, 1999) and GenBank Acc. No. AF226688, has been described above. Claim 26 requires that the promoter plus 5' terminal portion comprise SEQ ID NO: 22 or 23, and claim 28 requires that the 3' terminal portion comprises SEQ ID NO: 24. Neither Zhao nor Zhang disclose the identity of the strain of *B. mori* used to make the transgenic silkworms or from which the 5' and 3' terminal portions of the fib-H gene were isolated. As indicated above, the gene cassette in the transgenic silkworm comprises sequences corresponding to SEQ ID NOs: 22, 23, and 24. As a result, the gene cassette in the silkworm either comprises SEQ ID NOs: 22, 23, and/or 24, or comprises sequences that are nearly identical to it.

Zhou describes the sequencing of the fib-H gene of strain p50 contained on a BAC clone, the sequence of which is disclosed in AF226688.

It would have been obvious to one of skill in the art at the time the invention was made to have made the transgenic silkworm of Zhao from strain p50 using 5' and 3' targeting sequences from the fib-H gene of p50 because the sequences were well characterized, and in making the silkworm, one of skill in the art would have been assured that the flanking sequences in the targeting vector would have been identical to the target sequences in the genome of the p50 strain, and therefore would undergo homologous recombination in order to produce the silkworm of Zhao or a silkworm equivalent to that of Zhao. Since the cited art describes the methodology and materials required, one would have had a reasonable expectation of success to reproduce the

transgenic silkworm of Zhao or an equivalent transgenic silkworm in a p50 background. The resulting gene cassette in the transgenic silkworm would contain SEQ ID NOs: 22, 23, and 24.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe, Ph.D. whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Scott D. Priebe

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